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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,314	05/17/2005	David Wallach	WALLACH33	6672
1444 7590 09/25/2008 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			EXAMINER SWOPE, SHERIDAN	
			ART UNIT 1652	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/511,314	<b>Applicant(s)</b> WALLACH ET AL.	
	<b>Examiner</b> SHERIDAN SWOPE	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 20-25,66-70 and 72-101 is/are pending in the application.
- 4a) Of the above claim(s) 20-25,68,72,79,84,89,94 and 99 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 66,67,69,70,73-78,80-83,85-88,90-93,95-98,100 and 101 is/are rejected.
- 7) ☒ Claim(s) 66,67,69,70,73-78,80-83,85-88,90-93,95-98,100 and 101 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

Applicants' Request for Continuing Examination of June 30, 2008, in response to the Final Rejection mailed January 3, 2008, is acknowledged. It is acknowledged that applicants have amended Claims 20, 66, 69, 70, 73, and 76 and added Claim 77-101. Claims 20-25, 66-70, 72-101 are pending. Claims 20-25, 68, 71 and 72 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicants' argument that Claims 20 and 24 are generic claims encompassing the elected invention is found not to be persuasive. Applicants are reminded that their elected invention is directed to a method for treatment of a disease involving IL-2, rheumatoid arthritis, using the NIK polypeptide of SEQ ID NO: 18. Claims 20 and 24 recite the limitation of the disease NOT involving signaling via IL-2; therefore said claims are not encompassed by the elected invention. New Claims 79, 84, 89, 94, and 99 are herein withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 66, 67, 69, 70, and 73-78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are hereby considered.

***Claims-Objections***

Claims 66, 67, 69, 70, and 73-78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are object to for reciting non-elected subject matter, there being no allowable generic or linking claim.

Claims 66, 69, 70, 73, and 76 are objected to for the phrase "administering to a subject in need an amount effective to bind to *cyc* and inhibit *cyc*/NIK interaction, of a polypeptide comprising:", which is poor grammar. Said phrase would be better stated as "administering to a

Art Unit: 1652

subject in need an amount of a polypeptide effective to bind to *cyc* and inhibit *cyc*/NIK interaction, wherein the polypeptide comprises:"

Claim 66, line 3 is objected to for "activation of a cytokine", which should be "activation of a cytokine receptor".

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66, 67, 69, 70, 73-78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For Claims 66(b), 69(b), 70(b), 73(b), 76(b), 81, 86, 91, 96, and 101, the phrase "maintains at least ....sequence identity" renders the claim indefinite. It is unclear whether said phrase means "has at least ....sequence identity", "comprises at least ....sequence identity", or some other meaning. The skilled artisan would not know the metes and bounds of the recited invention. Claims 67, 74, 75, 77, 78, 80-83, 85-88, 90-93, 95, 97, 98, 100, as dependent from one or more of Claims 66(b), 69(b), 70(b), 73(b), 76(b), 81, 86, 91, 96, are indefinite for the same reason. For purposes of examination, it is assumed that "maintains at least ....sequence identity" means "has at least ....sequence identity".

For Claims 66, 69, 70, 73, 76, 77, 82, 87, 92, and 97, the phrase "pharmaceutically acceptable functional derivative" renders the claim indefinite. The specification discloses (pg 24, parg 2):

'The definition "functional derivatives" as herein used refers to derivatives which can be prepared from the functional groups present on the lateral chains of the amino acid moieties or on

Art Unit: 1652

the terminal N- or C-groups according to known methods and are comprised in the invention when they are pharmaceutically acceptable i.e. when they do not destroy the protein activity or do not impart toxicity to the pharmaceutical compositions containing them. Such derivatives include for example esters or aliphatic amides of the carboxyl-groups and N-acyl derivatives of free amino groups or O-acyl derivatives of free hydroxyl-groups and are formed with acyl-groups as for example alcanoyl- or aroyl-groups.'

Said disclosure is only exemplary. The skilled artisan would not know the metes and bounds of the recited invention. Claims 67, 74, 75, 81, 86, 91, 96, and 101 as dependent from one or more of Claims 66, 69, 70, 73, 76, 77, 82, 87, 92, and 97, are indefinite for the same reason.

Claims 67, 74, 75, 77, 78, 80-83, 85-88, 9093, 95, 98, 100 and 101 are rendered indefinite for improper antecedent usage as follows.

For each of Claims 67, 74, 75, 77, 78, 80-83, 85-88, 9093, 95, 98, 100 and 101 the phrase "A method according to claim ..." should be corrected to "The method according to claim ...".

### ***Claim Rejections - 35 USC § 112-First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### **Enablement**

Rejection of Claims 66, 67, 69, 70, and 73-76 under 35 U.S.C. 112, first paragraph/lack of enablement, for the reasons explained in the prior action, is maintained. Claims 77, 78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are herein rejected under 35 U.S.C. 112, first paragraph/lack of enablement, for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

Art Unit: 1652

(A) The claims have now been amended to insert additional structural detail. In all of the independent claims, the term "variant" has now been amended to specify that the variant maintains at least 90% sequence identity with (a) and maintains the ability thereof to bind to *cyc* and inhibit *cyc*/NIK interaction. Similarly, the term "functional derivative" has been amended to such that it must be pharmaceutically acceptable, that it is prepared from the functional groups present on the lateral chains of the amino acid moieties or on the terminal N- or C- groups in the polypeptide, and it must bind to *cyc* and inhibit *cyc*/NIK interaction.

(B) With respect to the diseases that can be treated, the present invention does not contend that any novel discoveries have been made in this regard. The relationship between *cyc*/NIK interaction and human pathologies has been studied in depth and is discussed in the background section of the present specification.

(C) With respect to claim 66, the present specification specifies exactly which cytokines have the common gamma chain in its receptor. Those of ordinary skill in the art are already well aware of which diseases involve the activation of such a cytokine in their pathogenesis. Thus, it would not take undue experimentation to determine such diseases as this was already known at the time. The same is true for the diseases being treated in claims 69, 70, 73 and 76.

(A) Reply: It is acknowledged that Claims 66, 69, 70, 73, and 76 have been amended to include additional structural and functional limitations for the administered polypeptide. Claim 67, 74, and 75, as dependent from Claims 66, 73, and 69, respectively, have also been so amended. However, the specification fails to enable the full scope of polypeptides to be used in the methods of Claims 66, 67, 69, 70, 73, or 74-77, 81, 82, 86, 87, 91, 92, 96, 97, and 101 for the following reasons. For Claims 66, 67, 69, 70, 73, or 74-77, 81, 82, 86, 87, 91, 92, 96, 97, and

Art Unit: 1652

101, the specification fails to provide sufficient guidance for the skilled artisan to make and use the genus of the pharmaceutically acceptable functional derivatives encompassed by each claim.

The specification discloses (pg 24, parag 2):

‘The definition "functional derivatives" as herein used refers to derivatives which can be prepared from the functional groups present on the lateral chains of the amino acid moieties or on the terminal N- or C-groups according to known methods and are comprised in the invention when they are pharmaceutically acceptable i.e. when they do not destroy the protein activity or do not impart toxicity to the pharmaceutical compositions containing them. Such derivatives include for example esters or aliphatic amides of the carboxyl-groups and N-acyl derivatives of free amino groups or O-acyl derivatives of free hydroxyl-groups and are formed with acyl-groups as for example alcanoyl- or aroyl-groups.’ (Examiner’s emphasis)

Thus, Claims 66, 67, 69, 70, 73-77, 81, 82, 86, 87, 91, 92, 96, 97, and 101 encompass the use of an essentially unlimited number of derivatives of variants of SEQ ID NO: 18, wherein the derivatives comprise an alteration at any one of the functional groups present on the lateral chains of the amino acid moieties or on the terminal N- or C-groups. As explained, above for the rejection of Claims 66, 67, 69, 70, 73-77, 81, 82, 86, 87, 91, 92, 96, 97, and 101 under 35 U.S.C. 112, second paragraph as being indefinite the specification fails to define the full scope of said genus of derivatives. And, the specification fails to enable the skilled artisan to make and use the full scope of said derivatives.

(B) Reply: The Examiner fails to see where the background section of the specification describes how the prior art teaches that binding of *cyc*/NIK affects any specific disease. If Applicants are aware of such teachings, an Information Disclosure Statement citing the prior art should be filed.

(C) Reply: It is acknowledged that the specification teaches that a *cyc* is a subunit of the IL-2, IL-4, IL-7, IL-9, IL-13, IL-15 and IL-21 receptor complexes (pg 9, parag 3). However,

Art Unit: 1652

said disclosure is not sufficient to enable the skilled artisan to make and use the full scope of the recited invention for the following reasons.

The claims encompass treating any known or unknown disease mediated by activating any cytokine receptor comprising a *cyc*, wherein the treating is with a NIK polypeptide. Neither the specification nor the prior art teach (i) all known and unknown cytokine receptors comprising a *cyc*, (ii) that all effects of activating a cytokine receptor comprising a *cyc* are mediated by *cyc*/NIK binding or NIK activation, (iii) all known and unknown diseases affected by a cytokine receptor comprising a *cyc*, or (iv) any disease that can be treated using an NIK polypeptide that binds to *cyc* and inhibits *cyc*/NIK binding.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method for treating any known or unknown disease mediated by activating any cytokine receptor comprising a *cyc*, wherein the treating is with a NIK polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

For these reasons and those explained in the prior actions, Claims 66, 67, 69, 70, 73-78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are rejected under 35 U.S.C. 112, first paragraph/lack of enablement.



**Written Description**

Rejection of Claims 66, 67, 69, 70, and 73-76 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. Claims 77, 78, 80-83, 85-88, 90-93, 95-98, 100, and 101 are herein rejected under 35 U.S.C. 112, first paragraph/ written description, for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following argument: As discussed hereinabove with respect to the enablement rejection, the claims have now been amended so as to define the variants, functional derivatives, circularly permuted derivatives, and fragments that can be used in the present invention in a manner that requires substantial structural identity to the main compound. This argument is not found to be persuasive for the reasons explained above in (A).

***Allowable Subject Matter***

No claims are allowable.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1652

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

### **Final Comments**

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/  
Primary Examiner, Art Unit 1652